

In the Claims:

Please amend the claims as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application:

1.-33. (Canceled)

34. (New) A hepatitis C virus (HCV) vaccine comprising at least two epitopes, each from a different hotspot epitope, wherein a hotspot epitope is defined as an epitope containing at least one of the following peptides:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
GYKVLVLNPSVAAT (SEQ ID NO:60),
AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14),
DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26),
GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMYVGGVEHRL (SEQ ID NO:132;
SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID
NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),,
AAWYELTPAETTVRLR (SEQ ID NO:4),
GQGWRL LAPITAYSQQTRGLLGCIV (SEQ ID NO:54),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDRDRSELSPLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93),
LINTNGSWHINRTALNCNDL (SEQ ID NO:84),
TTLGIGTVLDQAET (SEQ ID NO:125),
FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID
NO:42; SEQ ID NO:43; SEQ ID NO:44),
ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8),
AFCSAMYVGDLCSV (SEQ ID NO:5),
GVLFGLAYFSMVGNW (SEQ ID NO:56),
VVCCSMSYTWTGALITPC (SEQ ID NO:144),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and

TTLLFNILGGWVAAQ (SEQ ID NO:126).

35. (New) The HCV vaccine of claim 34, further defined as comprising at least three epitopes, each from a different hotspot epitope.

36. (New) The HCV vaccine of claim 34, further defined as comprising at least four epitopes, each from a different hotspot epitope.

37. (New) The HCV vaccine of claim 34, further defined as comprising at least five epitopes, each from a different hotspot epitope.

38. (New) The HCV vaccine of claim 34, further defined as comprising at least six epitopes, each from a different hotspot epitope.

39. (New) The HCV vaccine of claim 34, wherein the epitopes are at least two of:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
KFPGGGQIVGGVYLLPRRGPRL (SEQ ID NO:72), YLLPRRGPRL (SEQ ID NO:146), LPRRGPRL (SEQ ID NO:86), GPRLGVRAT (SEQ ID NO:50), RLGVRATRK (SEQ ID NO:103), GYKVLVLNPSVAAT (SEQ ID NO:60), AYAAQGYKVL (SEQ ID NO:9), AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14); DLMGYIPAV (SEQ ID NO:19), GYIPLVGAPL (SEQ ID NO:59), DLMGYIPLVGAPL (SEQ ID NO:25), CINGVCWTV (SEQ ID NO:17), GEVQVVSTATQSFLAT (SEQ ID NO:47), GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49), HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63), MWNFISGIQYLAGLSTLPGN (SEQ ID NO:94), NFISGIQYLAGLSTLPGNPA (SEQ ID NO:97), QYLAGLSTL (SEQ ID NO:101), HMWNFISGI (SEQ ID NO:61), VDYPYRLWHYPCTVNFTIFKVRMYVGGVEHRL (SEQ ID NO:132), DYPYRLWHYPCTVNFTIFKI (SEQ ID NO:35), DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36), VDYPYRLWHYPCTVNYTIFKIRMYVGGVEHRL (SEQ ID NO:135), DYPYRLWHYPCTVNYTIFKI (SEQ ID NO:38), DYPYRLWHY (SEQ ID NO:33), TVNYTIFKI (SEQ ID NO:129), TINYTIFK (SEQ ID NO:120), TVNFTIFKV (SEQ ID NO:127), HYPCTVNYTI (SEQ ID NO:67), HYPCTVNFTI (SEQ ID NO:66), RMYVGGVEHR (SEQ ID NO:106), AAWYELTPAETTVRLR (SEQ ID NO:4), TPAETTVRL (SEQ ID NO:121), GWRLLAPITAYSQQTRGLLGCIV (SEQ ID NO:57), TAYSQQTRGLLGCIV (SEQ ID NO:116), TAYSQQTRGLLG (SEQ ID NO:115), GQGWRL LAPITAYSQ (SEQ

ID NO:52), RLLAPITAY (SEQ ID NO:105), GQGWRLLAPITAYSQQTRGLLGCIV (SEQ ID NO:54), GQGWRLLAPITAYSQQTRGLLG (SEQ ID NO:53), AYSQQTRGLL (SEQ ID NO:16), AYSQQTRGL (SEQ ID NO:15), IGLGVLDILAGYGAGVAGALVAFK (SEQ ID NO:70), ILAGYGAGV (SEQ ID NO:71), VAGALVAFK (SEQ ID NO:131), GYGAGVAGAL (SEQ ID NO:58), VVCCSMSYWTGALITPC (SEQ ID NO:144), SMSYWTGALITP (SEQ ID NO:112), SMSYWTGAL (SEQ ID NO:111), SYWTGALI (SEQ ID NO:114), FTDNSSPPAVPQTFQV (SEQ ID NO:46), LEDRDRSELSPLLSTTEW (SEQ ID NO:80), LEDRDRSELSPLLST (SEQ ID NO:79), RSELSPLL (SEQ ID NO:108), ELSPLLST (SEQ ID NO:39), DRDRSELSPL (SEQ ID NO:32), LEDRDRSEL (SEQ ID NO:78), LEDRDRSEL (SEQ ID NO:78), YLVAYQATVCARAQAPPSWD (SEQ ID NO:149), YLVAYQATV (SEQ ID NO:148), MSTNPKPQRKTKRNTNR (SEQ ID NO:93), PQRKTKRNTNR (SEQ ID NO:99), QRKTKRNTN (SEQ ID NO:100), RKTKRNTNR (SEQ ID NO:102), MSTNPKPQR (SEQ ID NO:92), MSTNPKPQK (SEQ ID NO:91), INTNGSWHINRTALNCNDL (SEQ ID NO:84), NGSWHINRTALNCNDL (SEQ ID NO:98), LINTNGSWHI (SEQ ID NO:82), RTALNCNDL (SEQ ID NO:109), LINTNGSWHINRTALN (SEQ ID NO:83), SWHINRTALN (SEQ ID NO:113), TTIGIGTVLDQAET (SEQ ID NO:125), TTIGIGTV (SEQ ID NO:124), TILGIGTVAL (SEQ ID NO:119), FDSSVLCECYDAGAAWYE (SEQ ID NO:40; SEQ ID NO:44), FDSSVLCECYDAGCA (SEQ ID NO:45), VLCECYDAGA (SEQ ID NO:142), VVLCECYDAGAAWYE (SEQ ID NO:145), ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8), ARLIVFPDL (SEQ ID NO:7), RLIVFPDLGV (SEQ ID NO:104), RVCEKMALY (SEQ ID NO:110), AFCSAMYVGDLCSV (SEQ ID NO:5), GVLFGLAYFSMVGNW (SEQ ID NO:56), TRVPYFVRAQGLIRA (SEQ ID NO:123), TTLLFNILGGWVAAQ (SEQ ID NO:126), LLFNILGGWV (SEQ ID NO:85).

40. (New) The HCV vaccine of claim 34, further defined as comprising at least one epitope from at least three of the following hotspot epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
AYAAQGYKVLVLPNSVAAT (SEQ ID NO:14),
DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26),
GEVQVVSTATQSFLATCINGVCWT (SEQ ID NO:49), and
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

41. (New) The HCV vaccine of claim 40, further defined as comprising at least one epitope from at least four of the following hotspot epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
AYAAQGYKVLVLNPSVAAT (SEQ ID NO:14),
DLMGYIP(A/L)VGAPL (SEQ ID NO:25; SEQ ID NO:26),
GEVQVVSTATQSFLATCINGVCWTV (SEQ ID NO:49), and
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

42. (New) The HCV vaccine of claim 34, further defined as comprising at least one epitope from at least two of the following hotspot epitopes:

VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMYVGGVEHRL (SEQ ID NO:132;
SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID
NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),
AAWYELTPAETTVRLR (SEQ ID NO:4),
GQGWRL LAPITAYSQQTRGLLGCIV (SEQ ID NO:54),
IGLGKVLDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDRDRSELSPLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93) and
LINTNGSWHINRTALNCNDL (SEQ ID NO:84).

43. (New) The HCV vaccine of claim 42, further defined as comprising at least one epitope from at least three of the following hotspot epitopes:

VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMYVGGVEHRL (SEQ ID NO:132;
SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID
NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141),
AAWYELTPAETTVRLR (SEQ ID NO:4),
GQGWRL LAPITAYSQQTRGLLGCIV (SEQ ID NO:54),
IGLGKVLDILAGYGAGVAGALVAFK (SEQ ID NO:70),
FTDNSSPPAVPQTFQV (SEQ ID NO:46),
LEDRDRSELSPLLSTTEW (SEQ ID NO:80),
YLVAYQATVCARAQAPPPSWD (SEQ ID NO:149),
MSTNPKPQRKTKRNTNR (SEQ ID NO:93) and

LINTNGSWHINRTALNCNDSL (SEQ ID NO:84).

44. (New) The HCV vaccine of claim 43, further defined as comprising at least one epitope from at least four of the following hotspot epitopes:

VDYPYRLWHYPCT(V/I)N(F/Y)TIFK(V/I)RMYVGGVEHRL (SEQ ID NO:132; SEQ ID NO:133; SEQ ID NO:134; SEQ ID NO:135; SEQ ID NO:136; SEQ ID NO:137; SEQ ID NO:138; SEQ ID NO:139; SEQ ID NO:140; SEQ ID NO:141), AAWYELTPAETTVRLR (SEQ ID NO:4), GQGWRLLAPITAYSQQTRGLLGCIV (SEQ ID NO:54), IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), FTDNSSPPAVPQTFQV (SEQ ID NO:46), LEDRDRSELSPLLSTTEW (SEQ ID NO:80), YLVAYQATVCARAQAPPSWD (SEQ ID NO:149), MSTNPKPQRKTKRNTNR (SEQ ID NO:93) and LINTNGSWHINRTALNCNDSL (SEQ ID NO:84).

45. (New) The HCV vaccine of claim 34, further defined as comprising at least one epitope from at least two of the following hotspot epitopes:

TTILGIGTVLDQAET (SEQ ID NO:125), FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44), ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8), AFCSAMYVGDLCGSV (SEQ ID NO:5), GVLFGLAYFSMVGNW (SEQ ID NO:56), TRVPYFVRAQGLIRA (SEQ ID NO:123) and TTLLFNILGGWVAAQ (SEQ ID NO:126).

46. (New) The HCV vaccine of claim 45, further defined as comprising at least one epitope from at least three of the following hotspot epitopes:

TTILGIGTVLDQAET (SEQ ID NO:125), FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44), ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8), AFCSAMYVGDLCGSV (SEQ ID NO:5),

GVLFGLAYFSMVGKW (SEQ ID NO:56),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and
TTLLFNILGGWVAAQ (SEQ ID NO:126).

47. (New) The HCV vaccine of claim 46, further defined as comprising at least one epitope from at least four of the following hotspot epitopes:

TTLIGIGTVLDQAET (SEQ ID NO:125),
FDS(S/V)VLCECYDAG(A/C)AWYE (SEQ ID NO:40; SEQ ID NO:41; SEQ ID NO:42; SEQ ID NO:43; SEQ ID NO:44),
ARLIVFPDLGVRVCEKMALY (SEQ ID NO:8),
AFCSAMYVGDLDCGSV (SEQ ID NO:5),
GVLFGLAYFSMVGKW (SEQ ID NO:56),
TRVPYFVRAQGLIRA (SEQ ID NO:123) and
TTLLFNILGGWVAAQ (SEQ ID NO:126).

48. (New) The HCV vaccine of claim 34, further defined as comprising at least two of the following epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),
DLMGYIPAV (SEQ ID NO:19),
LEDRDRSELSPLLSTTEW (SEQ ID NO:80),
DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36),
GYKVLVLNPSVAAT (SEQ ID NO:60),
CINGVCWTW (SEQ ID NO:17),
AAWYELTPAETTVRLR (SEQ ID NO:4),
YLVAYQATVCARAQAPPSWD (SEQ ID NO:149),
TAYSQQTRGLLG (SEQ ID NO:115),
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),
IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), and
SMSYTWTGALITP (SEQ ID NO:112).

49. (New) The HCV vaccine of claim 48, further defined as comprising at least four of the epitopes.

50. (New) The HCV vaccine of claim 48, further defined as comprising at least five of the epitopes.

51. (New) The HCV vaccine of claim 48, further defined as comprising at least six of the epitopes.

52. (New) The HCV vaccine of claim 48, further defined as comprising at least eight of the epitopes.

53. (New) The HCV vaccine of claim 48, further defined as comprising all twelve of the epitopes.

54. (New) The HCV vaccine of claim 48, further defined as comprising at least two of the following epitopes:

KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73),

DYPYRLWHYPCTVNFTIFKV (SEQ ID NO:36),

AAWYELTPAETTVRLR (SEQ ID NO:4),

TAYSQQTRGLLG (SEQ ID NO:115),

HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63),

IGLGKVLVDILAGYGAGVAGALVAFK (SEQ ID NO:70), and

SMSYTWTGALITP (SEQ ID NO:112).

55. (New) The HCV vaccine of claim 54, further defined as comprising at least four of the epitopes.

56. (New) The HCV vaccine of claim 54, further defined as comprising at least five of the epitopes.

57. (New) The HCV vaccine of claim 54, further defined as comprising all seven of the epitopes.

58. (New) The HCV vaccine of claim 34, further defined as comprising the epitope KFPGGGQIVGGVYLLPRRGPRLGVRATRK (SEQ ID NO:73).

59. (New) The HCV vaccine of claim 34, further defined as comprising the epitope DLMGYIPAV (SEQ ID NO:19).

60. (New) The HCV vaccine of claim 34, further defined as comprising the epitope CINGVCWTV (SEQ ID NO:17).

61. (New) The HCV vaccine of claim 34, further defined as comprising the epitope HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

62. (New) The HCV vaccine of claim 34, further defined as comprising the epitope GYKVLVLNPSVAAT (SEQ ID NO:60).

63. (New) The HCV vaccine of claim 34, further defined as comprising the epitope VVCCSMSYTWTGALITPC (SEQ ID NO:144).

64. (New) The HCV vaccine of claim 34, further defined as comprising any two of the epitopes:

GYKVLVLNPSVAAT (SEQ ID NO:60),
CINGVCWTV (SEQ ID NO:17), and
HMWNFISGIQYLAGLSTLPGNPA (SEQ ID NO:63).

65. (New) The vaccine of claim 64, further defined as comprising all three of the epitopes.

66. (New) The vaccine of claim 65, further defined as comprising the epitope DLMGYIPAV (SEQ ID NO:19).

67. (New) The vaccine of claim 65, further defined as comprising the epitope KFPGGGQIVGGVYLLPRRGPRL (SEQ ID NO:72).

68. (New) The vaccine of claim 65, further defined as comprising the epitopes DLMGYIPAV (SEQ ID NO:19) and KFPGGGQIVGGVYLLPRRGPRL (SEQ ID NO:72).

69. (New) The HCV vaccine of claim 34, further defined as comprising a peptide (“Peptide A”) comprising a sequence R₁-X_ZX_NXZX-R₂, (SEQ ID NOS:152-156, where N is 3-7, respectively) wherein:

N is a whole number between 3 and 7;

X is a positively charged natural and/or non-natural amino acid residue;

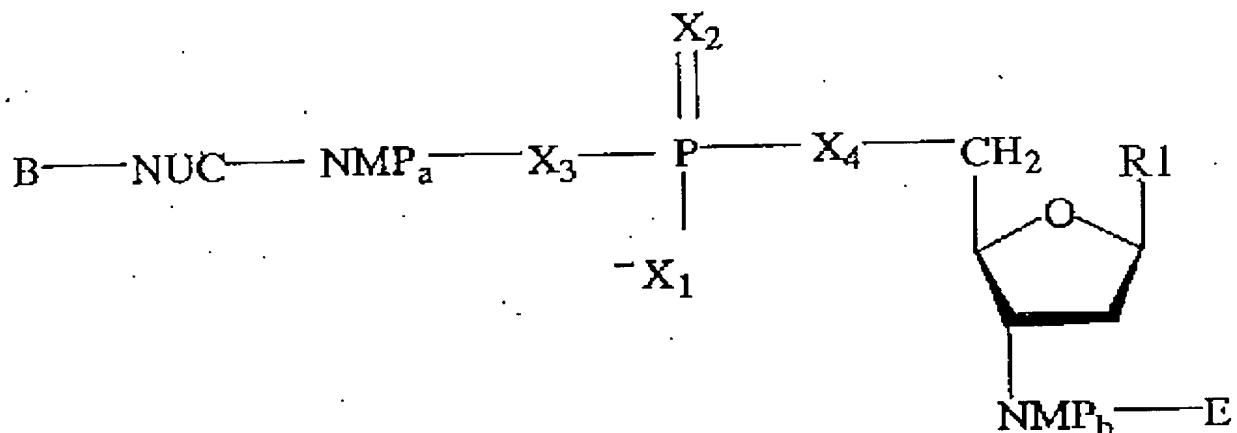
Z is an amino acid residue selected from the group consisting of L, V, I, F and/or W; and R₁ and R₂ are independently: -H, -NH₂, -COCH₃, -COH, a peptide with up to 20 amino acid residues or a peptide reactive group, or a peptide linker with or without a peptide; and

X-R₂ may be an amide, ester or thioester of the C-terminal amino acid residue of the peptide.

70. (New) The HCV vaccine of claim 69, wherein N is 5.

71. (New) The HCV vaccine of claim 69, wherein the sequence of Peptide A is KLKL_sKLK (SEQ ID NO:75).

72. (New) The HCV vaccine of claim 34, further defined as comprising an immunostimulatory oligodeoxynucleic acid molecule (ODN) having the structure according to the formula (I):



wherein

R₁ is selected from hypoxanthine and uracil;

any X is O or S;

any NMP is a 2' deoxynucleoside monophosphate or monothiophosphate, further defined as: deoxyadenosine-, deoxyguanosine-, deoxyinosine-, deoxycytosine-, deoxyuridine-, deoxythymidine-, 2-methyl-deoxyinosine-, 5-methyl-deoxycytosine-, deoxypseudouridine-, deoxyribosepurine-, 2-amino-deoxyribosepurine-, 6-S-deoxyguanine-, 2-dimethyl-deoxyguanosine-, or N-isopentenyl-deoxyadenosine-monophosphate or -monothiophosphate,

NUC is a 2' deoxynucleoside, further defined as deoxyadenosine-, deoxyguanosine-, deoxyinosine-, deoxycytosine-, deoxyguanosine-, deoxythymidine-, 2-methyl-deoxyuridine-, 5-methyl-deoxycytosine-, deoxypseudouridine-, deoxyribosepurine-, 2-amino-deoxyribosepurine-, 6-S-deoxyguanine-, 2-dimethyl-deoxyguanosine-, or N-isopentenyl-deoxyadenosine;

a and b are integers from 0 to 100 with the proviso that a + b is between 4 and 150;

and

B and E are common groups for 5' or 3' ends of nucleic acid molecules ("I-/U-ODN").

73. (New) The HCV vaccine of claim 72, wherein said I-/U-ODN is oligo d(IC)₁₃.

74. (New) The HCV vaccine of claim 34, further defined as comprising an Al(OH)₃ adjuvant.

75. (New) The HCV vaccine of claim 34, further defined as comprising a polycationic peptide.

76. (New) The HCV vaccine of claim 34, further defined as comprising an oligodeoxynucleotide containing a CpG-motif.

77. (New) The HCV vaccine of claim 34, further defined as being in a lyophilised form which is reconstitutable within 15 min. at 37°C.

78. (New) The HCV vaccine of claim 77, further defined as comprising traces of acetic acid.

79. (New) The HCV vaccine of claim 34, further defined as comprising between 20 µg and 10 mg of each epitope.

80. (New) The HCV vaccine of claim 34, further defined as comprising at least one A2 epitope, at least one DR1 epitope, at least one DR7 epitope, and/or or at least one of each of these epitopes.

81. (New) A method of treating a subject infected with HCV comprising administering to the subject a vaccine of claim 34.

82. (New) The method of claim 81, wherein the subject is a human.

83. (New) A method for the preparation of a vaccine of claim 34, comprising:
chemically synthesising the at least two epitopes of claim 34;
solubilising these epitopes by an aqueous solution containing at least one organic acid selected from the group consisting of formic acid, acetic acid, propionic acid, butyric acid and halogenated or hydroxylated forms thereof; and
mixing the solubilised epitopes.

84. (New) The method of claim 83, further comprising lyophilising the mixed epitopes.